

**MICROWAVE-INDUCED BISMUTH NITRATE-CATALYZED ELECTROPHILIC
SUBSTITUTION OF INDOLE WITH KETO ESTER UNDER SOLVENT-FREE
CONDITIONS**

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Abstract: Microwave-induced preparation of bis(indolyl)methane derivative has been developed through a bismuth nitrate-catalyzed reaction of indole with diethylketomalonate under solvent-free conditions.

Keywords: Microwave, Bismuth Nitrate, Indole

Introduction:

Indoles are used as medicinally active agents.¹ Bis(indolyl)alkanes are also very crucial as bioactive compounds. Many synthetic studies have been performed toward the synthesis of these types of molecules.^{2,3} Most of the cases excess protic acids or Lewis acids are used. The acid-catalyzed electrophilic reaction of indole with carbonyl compound is the most general method for the synthesis of bis(indolyl)methanes. Several catalysts, for example InCl_3 , $\text{In}(\text{OTf})_3$, $\text{Dy}(\text{OTf})_3$, InF_3 , $\text{Ln}(\text{OTf})_3$, acetic acid, LiClO_4 , TBATB, CuBr_2 , FeCl_3 , N-bromosuccinimide, KHSO_4 , $\text{NaHSO}_4 \cdot \text{SiO}_2$, CAN, clay, sulfamic acid, zeolites, $\text{H}_3\text{PMo}_{12}\text{O}_{40} \cdot x\text{H}_2\text{O}$ and trichloro-1,3,5-triazine were used.³ Similar reaction with activated diester is not known. The diester group in indole system can be converted to other functionalized bisindole derivatives. Therefore, studies of reaction between indole and an activated diester are important.

We report a microwave-induced method for the preparation of bis(indolyl)alkanes under solvent-free conditions by reacting indole with diethylketomalonate using catalytic amounts of bismuth nitrate (**Scheme 1**).

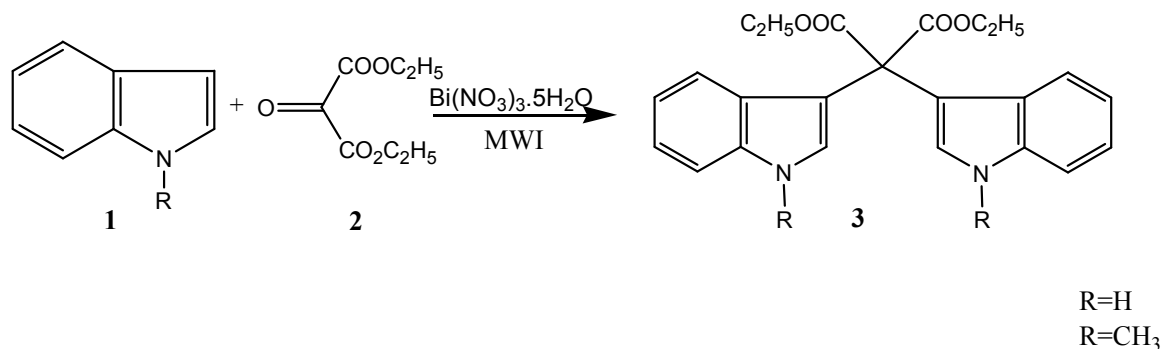
Results and Discussion:

Trivalent bismuth salts has been proved to be very useful in synthetic chemistry.⁴ We have developed various bismuth nitrate-mediated reactions that include nitration of aromatic compounds, protection of carbonyl functionality, deprotection of oximes and hydrazones, Michael addition and Paal-Knoor reaction. During this study, it has been conceived that bisindole derivatives can be easily prepared using bismuth nitrate.

Bismuth nitrate acts as a Lewis acid. Diethylketomalonate is an oil and this can be mixed with indole in the presence of bismuth nitrate as a paste in a reaction flask. Indole **1** and

diethylketomalonate **2** (2:1) were mixed in the presence of catalytic amounts of bismuth nitrate pentahydrate and the reaction mixture was irradiated in a domestic microwave oven.

Scheme 1



The results indicate that low power microwave irradiation can really produce the bis indole derivative **3** in excellent yield (75%). The reaction was completed within a few minutes. After the reaction, dichloromethane was added to the reaction mixtures, the organic layer was filtered and evaporated. The crude material was purified through a short column using silica gel and ethyl acetate-hexane (1:4) as the solvent.

Conclusion:

In conclusion, this method produces functionalized bis-indolylmethanes from indole in reasonably good yield. Our method using microwave-irradiation with catalytic amounts of bismuth nitrate is attractive for the synthesis of this novel type of molecule.

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